DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

JUN 1 2004

Via Federal Express

WARNING LETTER

Sandra Belmont, M.D., Director
LaserVision Correction Center and Corneal Service
Weill Medical College of Cornell University
525 East 68th Street
New York, NY 10021

Dear Dr. Belmont:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site. This letter discusses the violations identified during the inspection and requests that you implement prompt corrective actions. Investigators from the FDA's New York District Office, L. Glenn Massimilla, Ph.D.; Paul C. Mouris; Lisa Mathew; and Amy W. Yan conducted the inspection from January 13 through February 10, 2004. The purpose of the inspection was to determine if your activities as a clinical investigator for the "[redacted]: [redacted] System for [redacted] for [redacted] ([redacted])" study complied with applicable FDA regulations. The [redacted] is a device as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 321 (h)].

The FDA conducted the inspection under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. The program also ensures that human subjects are protected from undue hazard or risk during scientific investigations.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR), Part 812-Investigational Device Exemptions. At the close of the inspection, Dr. Massimilla presented a Form FDA 483 "Inspectional Observations" to you for review and discussed the listed deviations. The deviations noted on the FDA 483 and our subsequent inspection report review are discussed below.

(1) Failure to conduct the investigation according to the signed agreement with the sponsor, the investigational plan, and any conditions imposed by the Investigational Review Board (IRB). (21 CFR 812.100 and 812.110(b))

Under FDA regulations, you are required to conduct your clinical investigation in accordance with any conditions of approval imposed by the reviewing IRB. Our inspection revealed that an adverse event (excessive bleeding in an [redacted] from [redacted]) that occurred in June 2003 was not reported to the IRB within the IRB designated timeframe of 5 days; rather it was reported in February 2004. The adverse event was the result of failure to abide by the study protocol, which required that the subjects not be taking systemic medications. This subject was taking aspirin daily. The surgery was terminated and rescheduled for 24 days later.

You are also required to conduct your clinical investigation in accordance with the study protocol, which required the following parameters be used in treatment of the subjects: (1) depth of incision was to be about [redacted], (2) width of incision was to be [redacted]μ, and (3) [redacted] settings were specified as [redacted] and [redacted]. Our inspection revealed deviations from these parameters, including but not limited to the following:

- Ten subjects had at least one scleral incision of [redacted] or greater, which is beyond the depth specified.
- Where the case report form was adequately completed for this value, all subjects had incisions of at least [redacted], which was beyond the specified width.
- Two subjects were treated with settings of [redacted] and [redacted] and one subject was treated with the settings of [redacted] and [redacted] left [redacted] ([redacted]) and [redacted] and [redacted] right [redacted] ([redacted]). All of these values are beyond the settings specified in the protocol.
- Subject [redacted] and subject [redacted] were enrolled and treated despite meeting at least one exclusion criteria. Specifically, subject [redacted] had hypertension and was taking systemic medications and subject [redacted] was taking systemic medications, including an antihistamine.
- Subject [redacted] was cleared for treatment despite taking an antihistamine.

(2) Failure to maintain accurate, complete, and current records relating to the investigator's participation in an investigation, including records of each subject's case history and exposure to the device. (21 CFR 812.140(a)(3))

FDA regulations require investigators to maintain accurate, complete, and current records as described in 21 CFR 812.140(a). Included in these required records are documentation of each subject's case history and exposure to the investigational device. Our inspection revealed deviations from these requirements, including but not limited to the following:

- Medical records/case report forms reviewed had numerous write-over corrections which lacked dates and initials of the individuals making the corrections. For instance, for subject [redacted], the total energy used was crossed out and a different energy total was used. Subject [redacted] had cross-offs and changes noted under

frequency of intra-operative medications and the depth and energy of the cut at the 4:30 location was changed. Subject [redacted] had cross-off data in the [redacted] size field. Subject [redacted] had crossed-off data in the medication fields, the [redacted] setting field, the total energy field, and cut field.

- Most of the operative forms were missing data in the [redacted] size fields.
- On the case report form titled "Operative & Post Operative Record Examination," the required total energy entry was not completed for six subjects . On nine additional forms, the data recorded in the total energy field was incorrect in that the total energy did not match the sum of the energy when added for each individual cut.
- One subject record ([redacted]) did not contain any documentation of prescreening.
- There were no source documents in any subject record to confirm the inclusion criterion that subjects entering the study had stable refraction over one year prior to surgery.

(3) Failure to maintain accurate, complete, and current records relating to documents evidencing informed consent. (21 CFR 812.140(a)(3)(i))

Federal regulations require that the case history for each individual shall document that informed consent was obtained prior to participation in the study. In addition, on February 28, 2002, your IRB notified you that the IRB required informed consent be obtained prior to the screening process. However, all the enrolled subjects signed the informed consent form on the day of treatment. The signing of the consent form by subjects followed initial screening and preparation for the treatment by up to 8 months.

In the future, in order to better understand investigational study practices, you might consider attending and having your staff attend training sessions that focus on the operations of investigational studies. In addition, you will want to ensure that future studies in which you are involved have clearly identified the sponsor and clinical investigator responsibilities, have clearly identified protocols, and are well-monitored. There needs to be close cooperation and communication between all participants of the study including the sponsor, the IRB, the investigator, and staff.

We would like to remind you that as a clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations. You should refer to the regulations relevant to device studies, some of which were referenced above, in 21 CFR Part 812. You can refer to the following Internet web site for additional information:

Investigational Device Exemptions -
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm

The above-described deviations are not intended to be an all-inclusive list of deficiencies that may exist in this clinical study. It is your responsibility as a clinical investigator to adhere to each requirement of the Act and all applicable federal regulations.

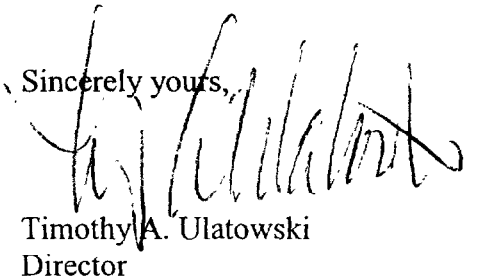
Within 15 working days after receiving this letter please provide written documentation of the specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 CFR 812.119.

Send your response to:

Food and Drug Administration,
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Program Enforcement Branch II, (HFZ-312)
2094 Gaither Road
Rockville, Maryland 20850
Attention: Mr. G. Levering Keely, BSN, MPA,
Consumer Safety Officer.

We are also sending a copy of this letter to FDA's New York District Office, 158-15 Liberty Avenue, Jamaica, NY, 11433, and request that you also send a copy of your response to that office. If you have any questions, please contact Mr. Levering Keely by phone at 301-594-4728 ext 142.

Sincerely yours,



Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health